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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,182	07/18/2001	Stefano Colloca	B-4175PCT 61	1087

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EXAMINER
WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/24/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/831,182	COLLOCA, STEFANO	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21, 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Amendment filed July 14, 2003 (Paper No. 20) in response to the Office Action of February 10, 2003 is acknowledged and has been entered. Claims 22, 23 and 27 have been cancelled. Claims 1-21 and 24-26 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on July 14, 2002 (Paper No.22), was received by the technology center in September 2003. The submission is in compliance with the provisions of 37 CFR 1.97. It appears that Applicants had submitted a copy of the listed references along with the IDS form 1449; however, in the process of getting the paper to the file the references have been misplaced by the office. Therefore, the references were not available to the examiner for review at the time of mailing the instant Office Action. Applicant is requested to supply an additional courtesy copy of all non-patent references so the examiner may consider them. Accordingly, the examiner will consider the information disclosure statement once all references have been located.

Specification

The office acknowledges the amendments to the specification.

Drawings

The office acknowledges the receipt of the corrected drawings; the drawings have been approved by Draftsperson's.

Claim Objections

The objection of claims 22 and 23 to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim **is withdrawn** in view of applicants cancellation of the claims.

Claim Rejections - 35 USC § 112

While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "genic" in the claims 1-27 is used by the claim to mean "genetic," while the accepted meaning in the context of the viral sequences is "polynucleotide sequence." According to Webster's dictionary the term "genic" refers to -of, relating to or being a gene-. The term genic unit in now interpreted to be a genetic unit and the rejection is herby **withdrawn**.

The rejection of claim 27 under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*,

255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966) **is withdrawn** in view of applicant's cancellation of the claim.

Claim Rejections - 35 USC § 102

The rejection of claim 22 under 35 U.S.C. 102(b) as being anticipated by Alemany et al. (Journal of Virological Methods, 1997) **is withdrawn** in view of applicant's cancellation of the claim.

The rejection of claim 23 under 35 U.S.C. 102(b) as being anticipated by Yeh et al. (Journal of Virology, 1996) **is withdrawn** in view of applicant's cancellation of the claim.

New Rejections:

Claim Rejections - 35 USC § 112

Claims 1-21 and 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically claim 1 refers to the first genic unit being an "adenovirus defective genome", it is not clear what specifically is encompassed by "defective" does this refer to the deletion of the minimal portion 600 bp needed for replication and encapsidation (see specification page 4, lines 39-36) or does this merely refer to the encapsidation signal and a non-structural region. Clarification of what is encompassed by the term is required.

In claims 8, 9, 18-21 the term "totally or partially constituted" in not clear, how much is derived from a human adenovirus and how much may derived from other viral genic units? The metes and bound of what is encompassed by the term in not clear because one of ordinary skill in the art would not know how much of one viral genic unit is needed. Clarification of what is encompassed by the term is required.

Claims 1-21 and 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using human adenoviral vectors and cell lines expressing human adenoviral constructs, does not reasonably provide enablement for adenoviruses derived from other species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The

quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention, the claims are drawn to the production of a helper dependent adenovirus vector using a cell line that provides the complementing factor needed to package the defective helper dependent vector. The claims are not limited to human adenoviruses and can include all animal viruses. The state of the prior art, indicates that there are significant differences between human adenoviruses (HAV) and porcine adenoviruses 3 (PAV3), because of these differences there is no reasonable expectation of success in applying the teaching of the instant specification which is drawn to human adenoviruses and apply them to porcine or bovine adenoviruses. PAV3 is very different to the human adenovirus at the genome (genic) level only approximately 54 % identity between PAV3 and HAV2 and HAV5 exists at the DNA level (see Gene Bank Accession #J01917, M73260 and AF083132). At the protein level the comparisons also show a significant difference. The PAV3 fiber protein has only 23.5 % identity with the HAV fiber protein, the PAV3 penton protein has about 58% identity with the HAV penton protein. These differences clearly show that PAV3 is very different to HAV in both genic and protein sequence content. The mere relationship of being in the same virus family or sharing the sharing of structural and function features does not provide one skilled in the art with the ability to manipulate a comparable sequence at the molecular level, to predict with reasonable success the structure and function of expressed proteins. (Tuboly et al. Restriction endonuclease analysis and physical mapping of the genome of porcine adenovirus type 5. Virus Research. 1995, Vol. 37, No. 1, pages 49-54). The construction of adenoviral vectors depends on utilizing homologous recombination events, this not only requires knowledge of the viral structural

sequences and their function, but also requires the appropriate cell line to carry out the recombination events.

There is no working example provided by the inventor demonstrating that the claimed cell line construction would be effective at packaging adenoviral vector from other species. A conclusion of lack of enablement means that, at the time the application was filed, the specification would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Due to the breadth of the claims encompassing all adenoviruses, the inability of the skilled artisan to a priori predict how to make the appropriate constructs for example in PAV3, the lack of direction provided by the inventor, and the lack of working examples, it is determined that an undue quantity of experimentation would be required for one skilled in the art to use the invention in its full scope.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER